

(200 mL). The organic layer was dried over sodium sulfate (50 g, powdered) for 2 h. The solution was filtered and concentrated under reduced pressure to a viscous oil. The resulting phosphoramidite was purified by silica gel flash chromatography (800 g, ethyl acetate-triethylamine 99:1). Selected fractions were combined, concentrated under reduced pressure, and dried at 25°C/0.2 mmHg for 16 h to give 18.0 g (46%, 3% from guanosine hydrate) of solid foam TLC homogenous. ³¹P-NMR (CDCl₃, H₃PO₄ std.) δ 147.96; 148.20 (diastereomers).

EXAMPLE 9

5'-O-DMT-3'-O-(2-methoxyethyl)-5-methyl-uridine-2'-O-succinate

[0144] 5'-O-DMT-3'-O-(2-methoxyethyl)-thymidine was first succinylated on the 2'-position. Thymidine nucleoside (4 mmol) was reacted with 10.2 mL dichloroethane, 615 mg (6.14 mmol) succinic anhydride, 570 μL (4.09 mmol) triethylamine, and 251 mg (2.05 mmol) 4-dimethylaminopyridine. The reactants were vortexed until dissolved and placed in heating block at 55 °C for approximately 30 minutes. Completeness of reaction checked by thin layer chromatography (TLC). The reaction mixture was washed three times with cold 10% citric acid followed by three washes with water. The organic phase was removed and dried under sodium sulfate. Succinylated nucleoside was dried under P₂O₅ overnight in vacuum oven.

EXAMPLE 10

5'-O-DMT-3'-O-methoxyethyl-5-methyl-uridine-2'-O-succinoyl Linked LCA CPG 5'-O-DMT-3'-

[0145] O-(2-methoxyethyl)-2'-O-succinyl-thymidine was coupled to controlled pore glass (CPG).

1.09 g (1.52 mmol) of the succinate were dried overnight in a vacuum oven along with 4-dimethylaminopyridine (DMAP), 2,2'-dithiobis (5-nitro-pyridine) (dTNP), triphenylphosphine (TPP), and pre-acid washed CPG (controlled pore glass). After about 24 hours, DMAP (1.52 mmol, 186 mg) and acetonitrile (13.7 mL) were added to the succinate. The mixture was stirred under an atmosphere of argon using a magnetic stirrer. In a separate flask, dTNP (1.52 mmol, 472 mg) was dissolved in acetonitrile (9.6 mL) and dichloromethane (4.1 mL) under argon. This reaction mixture was then added to the succinate. In another separate flask, TPP (1.52 mmol, 399 mg) was dissolved in acetonitrile (37 mL) under argon. This mixture was then added to the succinate/DMAP/dTNP reaction mixture. Finally, 12.23 g pre-acid washed LCA CPG (loading = 115.2 $\mu\text{mol/g}$) was added to the main reaction mixture, vortexed shortly and placed on shaker for approximately 3 hours. The mixture was removed from the shaker after 3 hours and the loading was checked. A small sample of CPG was washed with copious amounts of acetonitrile, dichloromethane, and then with ether. The initial loading was found to be 63 $\mu\text{mol/g}$ (3.9 mg of CPG was cleaved with trichloroacetic acid, the absorption of released trityl cation was read at 503 nm on a spectrophotometer to determine the loading.) The whole CPG sample was then washed as described above and dried under P_2O_5 overnight in vacuum oven. The following day, the CPG was capped with 25 mL CAP A (tetrahydrofuran/acetic anhydride) and 25 mL CAP B (tetrahydrofuran/pyridine/1-methyl imidazole) for approximately 3 hours on shaker. Filtered and washed with dichloromethane and ether. The CPG was dried under P_2O_5 overnight in vacuum oven. After drying, 12.25 g of CPG was isolated with a final loading of 90 $\mu\text{mol/g}$.

EXAMPLE 11**3'-O-Methoxyethyl-5-methyl-N-benzoyl-cytidine-2'-O-succinate**

[0146] 5'-O-DMT-3'-O-(2-methoxy) ethyl-N-benzoyl-cytidine was first succinylated on the 2'-position. Cytidine nucleoside (4 mmol) was reacted with 10.2 mL dichloroethane, 615 mg (6.14 mmol) succinic anhydride, 570 μ L (4.09 mmol) triethylamine, and 251 mg (2.05 mmol) 4-dimethylaminopyridine. The reactants were vortexed until dissolved and placed in a heating block at 55 °C for approximately 30 minutes. Completeness of reaction was checked by thin layer chromatography (TLC). The reaction mixture was washed three times with cold 10% citric acid followed by three washes with water. The organic phase was removed and dried under sodium sulfate. The succinylated nucleoside was dried under P_2O_5 overnight in vacuum oven.

EXAMPLE 12**5'-O-DMT-3'-O-methoxyethyl-5-methyl-N-benzoyl-cytidine-2'-O-succinoyl linked LCA CPG**

[0147] 5'-O-DMT-3'-O-(2-methoxyethyl)-2'-O-succinyl-N⁴-benzoyl cytidine was coupled to controlled pore glass (CPG). 1.05 g (1.30 mmol) of the succinate were dried overnight in a vacuum oven along with 4-dimethylaminopyridine (DMAP), 2,2'-dithiobis (5-nitro-pyridine) (dTNP), triphenylphosphine (TPP), and pre-acid washed CPG (controlled pore glass). The following day, DMAP (1.30 mmol, 159 mg) and acetonitrile (11.7 mL) were added to the succinate. The mixture was "mixed" by a magnetic stirrer under argon. In a separate flask, dTNP (1.30 mmol, 400 mg) was dissolved in acetonitrile (8.2 mL) and dichloromethane (3.5 mL) under argon. This reaction mixture